

Docket No.: 2870-0319PUS1  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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In re Patent Application of:  
Hideo TASHIRO et al.

Application No.: 10/560,584

Confirmation No.: 6678

Filed: December 13, 2005

Art Unit: N/A

For: SUBSTRATE FOR BIOMOLECULE  
MICROARRAY, BIOMOLECULE  
MICROARRAY, DEVICE AND METHOD OF  
PROMOTING INTERACTION AND METHOD  
OF DETECTING INTERACTION (as amended)

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Examiner: Not Yet Assigned

**LETTER**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Subsequent to the filing of the above-identified application on December 13, 2005, attached hereto is an English translation of the International Preliminary Report on Patentability (Form PCT/IB/373) that should be made of record in the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or to credit any overpayment to Deposit Account No. 02-2448 for any

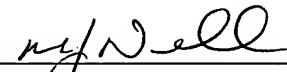
Application No.: 10/560,584

Docket No.: 2870-0319PUS1

additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Dated: May 23, 2006

Respectfully submitted,

By 

Mark J. Nuell, Ph.D.

Registration No.: 36,623

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Attorney for Applicant

Attachment(s)

From the INTERNATIONAL BUREAU

**PCT**

NOTIFICATION OF TRANSMITTAL  
OF COPIES OF TRANSLATION  
OF THE INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY  
(CHAPTER I OR CHAPTER II  
OF THE PATENT COOPERATION TREATY)  
(PCT Rules 44bis.3(c) and 72.2)

To:

SIKs & Co.  
8th Floor, Kyobashi-Nisshoku Bldg.  
8-7, Kyobashi 1-chome  
Chuo-ku, Tokyo 1040031  
JAPON

Date of mailing ( <i>day/month/year</i> ) 04 May 2006 (04.05.2006)	
Applicant's or agent's file reference A45123H	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/JP2004/008413	International filing date ( <i>day/month/year</i> ) 09 June 2004 (09.06.2004)
Applicant RIKEN et al	

## 1. Transmittal of the translation to the applicant.



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

## 2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

## 3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 90 90

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference A45123H	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/JP2004/008413	International filing date ( <i>day/month/year</i> ) 09 June 2004 (09.06.2004)	Priority date ( <i>day/month/year</i> ) 13 June 2003 (13.06.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant RIKEN		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).																								
2.	This REPORT consists of a total of 7 sheets, including this cover sheet.  In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 60%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input checked="" type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement																							
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<input type="checkbox"/>	Box No. VII	Certain defects in the international application																							
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 740 14 35	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 5px;">Date of issuance of this report 24 April 2006 (24.04.2006)</td> </tr> <tr> <td style="padding: 5px;">Authorized officer  Yoshiko Kuwahara</td> </tr> <tr> <td style="padding: 5px;">Telephone No. +41 22 338 90 90</td> </tr> </table>	Date of issuance of this report 24 April 2006 (24.04.2006)	Authorized officer  Yoshiko Kuwahara	Telephone No. +41 22 338 90 90
Date of issuance of this report 24 April 2006 (24.04.2006)				
Authorized officer  Yoshiko Kuwahara				
Telephone No. +41 22 338 90 90				

# PATENT COOPERATION TREATY

TRANSLATION

PCT

From the  
INTERNATIONAL SEARCHING AUTHORITY

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing  
(day/month/year)

Applicant's or agent's file reference

**A45123H**

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.

**PCT/JP2004/008413**

International filing date (day/month/year)

**09.06.2004**

Priority date (day/month/year)

**13.06.2003**

International Patent Classification (IPC) or both national classification and IPC

Applicant

**RIKEN**

1. This opinion contains indications relating to the following items:

- |                                     |              |                                                                                                                                                                      |
|-------------------------------------|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion                                                                                                                                                 |
| <input type="checkbox"/>            | Box No. II   | Priority                                                                                                                                                             |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                     |
| <input checked="" type="checkbox"/> | Box No. IV   | Lack of unity of invention                                                                                                                                           |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited                                                                                                                                              |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application                                                                                                                     |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application                                                                                                                |

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/IP

Authorized officer

Facsimile No.

Telephone No.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2004/008413

Box No. 1      Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language  
\_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

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Box No. IV

Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
- ☐ paid additional fees
- ☐ paid additional fees under protest
- ☐ not paid additional fees
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with
- ☒ not complied with for the following reasons:

"The special technical feature" of the inventions of claims 1-27 is a biological microarray substrate, wherein a spot for fixing a biomolecule protrudes from the substrate surface and a plane for the spot is provided on top thereof.

"The special technical feature" of the inventions of claims 28-30 is in that at least one buffer substance selected from the group including phenyl alanine, histidine, carnosine, and arginine, is introduced into the solution comprising the target biomolecule when interaction of the biomolecule fixed to the substrate surface of the microarray and the target biomolecule is induced by electrophoresis.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

- ☒ all parts
- ☐ the parts relating to claims Nos. \_\_\_\_\_

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/JP2004/008413
----------------------------------------------------

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	2, 3, 7, 9, 12-30	YES
	Claims	1, 4-6, 8, 10, 11	NO
Inventive step (IS)	Claims	2, 3, 22-30	YES
	Claims	1, 4-21	NO
Industrial applicability (IA)	Claims	1-30	YES
	Claims		NO
2. Citations and explanations:			
<p>Document 1: JP 2003-514227 A (Clinical Micro Sensors Incorporated), 15 April 2003 &amp; WO 01/35100 A &amp; EP 1254372 A</p> <p>Document 2: JP 11-127900 A (Commissariat a l'Energie Atomique), 18 May 1999 &amp; EP 0890651 A &amp; US 6255677 B1</p> <p>Document 1 describes "a substrate for a biosensor in which the substrate 30 has a first electrophoresis electrode 10, the electrophoresis electrode 10 has an array of detection electrodes 20 thereupon, and a nucleic acid is bonded to the detection electrodes 20", that "bonding of the target analyte to the trapping ligand is enhanced by conducting electrophoresis by using the counter electrode 50", that "the preferred electrode is from gold, platinum, silicon, carbon, and metal oxides", and that "the adequate substrate is from glass, silicon, or plastic. Furthermore, Fig. 1 shows "that the angle formed by the top plate and side surface of the detection electrode 20 is a right angle".</p> <p>Document 2 describes "a DNA chip comprising heating means for each electrode".</p> <p>The inventions of claims 1, 4 to 6, 8, 10, and 11 do not appear to possess novelty based on document 1 (see Abstract, Par. Nos. 0005, 0022, 0024, 0044, 0062, 0084, Fig. 1) cited in the ISR.</p> <p>The invention of claim 7 does not appear to involve an inventive step based on document 1 cited in the ISR. Optimizing the numerical range is merely the demonstration of the usual creative capacity of a person skilled in the art, and setting the height of the protruding spot section to 10-500 µm can be done as appropriate by a person skilled in the art.</p> <p>The invention of claim 9 does not appear to involve an inventive step based on document 1 cited in the ISR. Roughening the adsorption surface in the invention described in document 1 can be done as appropriate by a person skilled in the art.</p>			

Continued (1/3)

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: V.2

The inventions of claims 12-14, 19 do not appear to involve an inventive step based on document 1 cited in the ISR. The substrate for a biosensor in the invention described in document 1 is a substrate in which bonding of the target analyte with a trapping ligand located on the detection electrodes 20 is enhanced by electrophoresis, and using a configuration in which a terminal capable of supplying electric current to the detection electrodes 20 is provided on the substrate surface in order to generate an electric field for electrophoresis, providing a first electrophoresis electrode 10 and detection electrodes 10 as an integral electrically conductive substance cover layer, and disposing a solution containing target biomolecules between the substrate for a biosensor and the counter electrode 50 and inducing the interaction of biomolecules by applying an electric field between the microarray and the counter electrode could be done as appropriate by a person skilled in the art.

The invention of claim 15 does not appear to involve an inventive step based on document 1 cited in the ISR. Optimizing the numerical range is merely the demonstration of the usual creative capacity of a person skilled in the art, and setting the distance between the plane for a spot and the electrode to 1-500  $\mu\text{m}$  can be done as appropriate by a person skilled in the art.

The invention of claim 16 does not appear to involve an inventive step based on document 1 cited in the ISR. Providing a nonconductive spacer between the electrodes for electrophoresis could be done as appropriate by a person skilled in the art.

The invention of claim 17 does not appear to involve an inventive step based on document 1 cited in the ISR. Document 1 describes using tin indium oxide as the electrodes (see Par. No. 0062). Because the tin indium oxide is a transparent electrically conductive substance, a person skilled in the art would not find it difficult to produce the counter electrode 50 from indium tin oxide, thereby producing a transparent electrode, in the invention described document 1.

The invention of claim 18 does not appear to involve an inventive step based on document 1 and document 2 (see Abstract) cited in the ISR. Providing means for heating each electrode described in the invention of document 2 in the substrate for a biosensor described in document 1 could have easily been done by a person skilled in the art.

The invention of claim 20 does not appear to involve an inventive step based on document 1 cited in the ISR. Optimizing the numerical range is merely the demonstration of the usual creative capacity of a person skilled in the art, and setting the electric field applied between the microarray and the electrodes to 0.001-10 MV/m can be done as appropriate by a person skilled in the art.

The invention of claim 21 does not appear to involve an inventive step based on document 1 cited in the ISR. Using a nucleic acid that is a detection object as a fluorescent indicator would be done as appropriate by a person skilled in the art. Continued (1/3)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2004/008413

Supplemental Box

In case the space in any of the preceding boxes is not sufficient

Continuation of: V.2

Providing an almost V-shaped substrate surface on the circumference of the protruding spot section in the invention of claim 2 is described in none of the documents cited in the ISR and is not obvious to a person skilled in the art.

Using a configuration of the adjacent protruding spot section with adjoining side surfaces of the invention of claim 3 is described in none of the documents cited in the ISR and is not obvious to a person skilled in the art.

The inventions of claims 23-27 relate to a substrate for a biomolecule microarray wherein a spot for fixing a biomolecule protrudes from the substrate surface, a flat surface for a spot is provided at the top thereof, and at least the substrate surface around the protruding spot section, side surface of the protruding spot section, and flat surface of the spot are from an electrically conductive substance, wherein the interaction between the biomolecule located on the fixing spot and the target biomolecule is detected with a detector of the co-focal point type; those features are not described in the documents cited in the ISR and are not obvious to a person skilled in the art.

Using at least one buffer substance selected from the group including phenyl alanine, histidine, carnosine, and arginine, in the solution comprising the target biomolecule when the interaction of the biomolecule fixed on the microarray and the biomolecule in the target solution is induced by electrophoresis, as in the inventions of claims 22 and 28-30, is not described in the documents cited in the ISR and is not obvious to a person skilled in the art.

End (3/3)